Symbol	Name	Synonyms	Organism
Ngfr	Tumor necrosis factor receptor superfamily member 16 precursor	LNGFR, Low-affinity nerve growth factor receptor, Low affinity neurotrophin receptor p75NTR, NGF receptor, p75, p75NGFR, p75NTR, Tnfrsf16	Mus musculus

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By immunohistochemistry, **p75NTR** alone was strongly expressed in TUNEL+/Bcl2- keratinocytes of the regressing outer root sheath, but both **p75NTR** and TrkB and/or TrkC were expressed by the nonregressing TUNEL-/Bcl2+ secondary hair germ keratinocytes.

Following engraftment, TNF-R-positive cells (i.e. p55 by keratinocytes; p75 by epidermal dendritic cells) were identified throughout the epidermis.

NADE specifically **binds** to the cell-death domain of **p75NTR**.

Furthermore, **p75NTR regulates** RhoA activity to mediate filopodial dynamics.

This study suggests that **p75NTR** may be a promising antisense **target** in the treatment of ALS.

This up-regulation of bradykinin **binding** sites did not occur in neurons from mice lacking **p75NTR** or in neurons from wild-type mice treated with p75NTR-blocking antibody, indicating that tyrosine kinase receptors alone are not sufficient to trigger this physiological neuronal response.

Thus, **p75NTR induces** death regardless of the presence or absence of TrkA expression.

This expression of **p75NTR** by epithelial **target** cells required NT-3 but not adult innervation.

In transfected cells, **p75NTR activated** RhoA, and neurotrophin binding abolished RhoA activation.

Concept & implementation
by Robert Hoffmann

The in vivo kinetics of appearance of p75 **binding** activity paralleled the accumulation of R2 mRNA.

We now report that at least some mouse p75 appears to exist as a disulfide-**linked** heterodimer with a subunit of Mr 22,000 (p22).

Furthermore, they are also consistent with the putative role of Necdin in signaling events **promoted** by **p75NTR** during mouse nervous system development.

Overall, our results indicate an essential role for **p75NTR** in supporting NGF-**triggered** TrkA signaling pathways mediating neuronal survival in hippocampal neurons.

Recently, Necdin and other MAGE proteins were found to **interact** in vitro with the intracellular domain of the **p75NTR** neurotrophin receptor, but this interaction has not been validated in vivo.

The neurotrophin-3-induced cell migration was also observed in Schwann cells isolated from sciatic nerves of **p75NTR**-/- mice, indicating that neurotrophin 3 **enhances** cell migration through TrkC.

On the one hand, **p75NTR** provides a positive modulatory **influence** on nerve growth factor (NGF) signaling through the high affinity neurotrophin receptor TrkA, and hence increases NGF survival signaling.

RNA analysis revealed that NGF mRNA was expressed in the pregnant uterus on day 7.5 p.c., mainly in the decidua, but it could not be detected in the EPC. **p75NGFR** mRNA was expressed in the EPCs, whereas TrkA mRNA was not detected in the placental tissues throughout day 7.5 to 10.5 p.c. We therefore conclude that maternally derived NGF may play a role in mouse placentation by **promoting** the giant-cell transformation of trophoblast cells through **p75NGFR**.

The possible role of p75 in the **enhanced** response to EGF seen in c-src overexpressers is discussed.

Identification of tumor necrosis factor (TNF) amino acids crucial for **binding** to the murine p75 TNF receptor and construction of receptor-selective mutants.

The zinc finger protein NRIF (neurotrophin receptor **interacting** factor) was originally identified by virtue of its interaction with the neurotrophin receptor **p75NTR** and its participation in embryonic apoptosis.

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In vitro, neurotrophin 3 **binding** to **p75NTR** increases neurite length and filopodial formation of immunopurified subplate neurons, suggesting a role for **p75NTR** in subplate growth cone morphology and function in vivo.

Gene expression for **p75NGFR** was detected in late-meiotic spermatocytes and early spermatids and was found to be **co-expressed** with trkB and trkC, two tyrosine kinase receptors, commonly regarded as the high-affinity receptors for brain-derived neurotrophic factor and neurotrophin-3.

Neurotrophin effects on neuroblastoma cells: correlation with trk and **p75NTR** expression and **influence** of Trk receptor bodies.

Co-expression of NADE and **p75NTR** **induced** caspase-2 and caspase-3 activities and the fragmentation of nuclear DNA in 293T cells.

In Chinese hamster ovary cells, inhibitors of the MEK/ERK and p38 MAP kinase pathways uncovered distinct signaling pathways required for the constitutive and **stimulated** shedding of **p75NTR**.

We now show that nerve growth factor but not brain-derived neurotrophic factor or neurotrophin-3 selectively increases the expression of bradykinin **binding** sites on cultured dorsal root ganglion neurons from adult mouse via **p75NTR**.

However, in contrast to WldS mice, in IL-6(-/-) mice we observed the characteristic lesion-**induced** invasion of macrophages and the upregulation of low-affinity neurotrophin receptor p75 (p75LNTR) mRNA levels identical to those of IL-6(+/+) mice.

In contrast, overexpression of Rab13 mutants impaired the **transport** of Claudin-1, but not LDLR and **p75NTR**.

In this report, we provide evidence that NGF and BDNF have functionally antagonistic actions on sympathetic neuron growth and target innervation, with NGF acting via TrkA to **promote** growth and BDNF via **p75NTR** to inhibit growth.

c-jun is essential for sympathetic neuronal death **induced** by NGF withdrawal but not by p75 activation.

p75 neurotrophin receptor signaling **regulates** growth cone filopodial dynamics through modulating RhoA activity.

Nerve growth factor regulates the expression of bradykinin **binding** sites on adult sensory neurons via the neurotrophin receptor p75.

Antibodies that block binding of NGF to the p75 receptor prevented NGF-**induced** NF-kappaB activation and reduced the NGF survival response to the same extent as superrepressor IkappaB-alpha.

Furthermore, p75 mutant neurons display reduced levels of **activated** RhoA compared with wild-type counterparts, consistent with the enhanced filopodial lengths observed on mutant growth cones.

Despite the reduced neurotrophin transport, cholinergic neurons of p75 nerve growth factor receptor-deficient mice were larger than **controls** and had an apparently normal density of immunostaining for choline acetyltransferase.

Immunoprecipitation of MYB proteins with an antiserum specific for exons 8 and 9 revealed a 74 kDa protein which co-precipitated and appeared to be **complexed** with p75 in normal hematopoietic cells and with the 48 kDa product of v-myb in leukemic cells.

Both exogenous and autocrine BDNF mediate this **effect** via **p75NTR** because (1) BDNF does not inhibit growth of neurons lacking **p75NTR**, (2) function-blocking **p75NTR** antibodies enhance NGF-mediated growth, and (3) **p75NTR**-/- sympathetic neurons grow more robustly in response to NGF than do their wild-type counterparts.

Mol. Cell. Biol., 11, 5113-5124), and that its phosphotyrosine content is increased cooperatively by c-src overexpression and EGF stimulation. p75 is rapidly (within 2 min) **phosphorylated** on tyrosine upon EGF treatment and undergoes a second, prolonged phase of tyrosyl phosphorylation from 7 to 21 h after EGF addition, suggesting that tyrosyl phosphorylation of p75 is important for late as well as early events following EGF receptor activation.

The p75 neurotrophin receptor **influences** NT-3 responsiveness of sympathetic neurons in vivo.

The p75 neurotrophin receptor has been implicated in neurotrophin **binding** and signaling for both NGF and NT3.

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Surprisingly, most sets of trkA-dependent sensory innervation are suppressed by trkB perhaps **interacting** with p75.

In addition, necdin and MAGE-G1 **interacted** with the p75 neurotrophin receptor via its distinct intracellular domains.

Levels of nerve growth factor and neurotrophin-3 are **affected** differentially by the presence of p75 in sympathetic neurons in vivo.

In the presence of a mild detergent, the Fgr was **co-immunoprecipitated** with a 75 kDa protein (p75) and several other molecules expressed on the cell surface membrane.

Both antibody were found to synergize on 4AS cells, as a result of a cooperative mechanism in which 33B3.1 blocks the formation of the high affinity complex hence allowing TU27 to bind with higher affinity, and TU27 blocks IL-2 **binding** to the p75 chain.

We describe a novel 75 Kd sequence-specific cytoplasmic factor (p75) that **binds** selectively to a 83-nucleotide 3'-untranslated region of R2 mRNA and did not bind to the 5'UTR, the coding region of the R2 message or to the 3'UTRs of other mRNAs (from c-myc, GM-CSF and the iron responsive element from the transferrin receptor mRNA), or to the homopolymer poly(A) sequence. p75-RNA binding activity, which requires new protein synthesis, is not present in untreated cells, but is induced following TGF-beta 1 stimulation.

P75 **interacts** with the Nogo receptor as a co-receptor for Nogo, MAG and OMgp.

In contrast, both p55 and p75 mAbs individually **blocked** development of skin necrosis in mice treated with murine TNF-alpha.

GM-6001 also inhibited the release of soluble TNF receptor (p75) from peripheral blood mononuclear cells **stimulated** with endotoxin and/or TNF alpha.

Quantitative RT-PCR analysis further showed that upregulation of TNF-alpha **transport** was related to increased expression of mRNA for p55 and p75 receptors.

Results indicated that both P55 and P75 receptors are required for FB1-**induced** hepatotoxicity and TNFalpha plays an important role in such response in mouse liver.

In contrast, brain-derived neurotrophic factor (BDNF) **binding** to p75 resulted in an equivalent level of apoptosis in neurons expressing Cre, GFP, and uninfected cells.

This study tests the specific role of p55 and p75 receptors in mediating the **transport** of TNF-alpha across the blood-spinal cord barrier (BSCB) after SCI by compression.

In ob/ob mice, p55 and p75 tumor necrosis factor-alpha receptors (TNFRs) act cooperatively to **induce** PAI-1 mRNA in most tissues, including the adipose tissue, kidney, heart, and liver.

IL-4 **induces** IL-2 receptor p75 beta-chain gene expression and IL-2-dependent proliferation in mouse T lymphocytes.

These data suggest that the amino terminal region of the IL 2 molecule **interacts** with the p75 chain of the IL 2 receptor.

Deletion of TNFR2 (p75) did not have an **effect**; deletion of TNFR1 (p55) reduced the diffuse microglial staining for MHC1-IR but did not abolish the MHC1(+) microglial nodules.

Nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and neurotrophin-3 (NT-3) selectively **bind** to distinct members of the Trk family of tyrosine kinase receptors, but all three bind with similar affinities to the neurotrophin receptor p75 (p75NTR).

These results suggest that necdin and MAGE-G1 **target** both E2F1

and p75 to regulate cell viability during brain development.

Combined stimulation with IFN-gamma/LPS enhances IL-12 p40 secretion and **induces** IL-12 p75 secretion by microglia.

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Two inhibitors of anti-CD3 induced TNF release; steroids and pentoxifylline both reduced TNF levels and P75 levels without **affecting** P55 levels.

IL-12 dimer formation appears to be reduced by NAC also in vivo, because pretreatment with NAC (1 g/kg, orally), before LPS injection in mice, inhibited peak IL-12 p75 serum levels without **affecting** those of p40.

The detection of p75 receptors in the mesenchyme implies that neurotrophins are likely to exert **effects** during morphogenesis of mesodermal tissues and that separate signals are likely to direct neuronal versus nonneuronal expression of the p75 gene.

TU27, a mouse IgG1 mAb directed at the p75 chain of the human IL-2R, was analyzed for its ability to interact with IL-2 **binding** on isolated p75 chains (YT-2C2 cells) and high affinity p55/p75 receptors (human alloreactive T cell clone 4AS), to inhibit IL-2-induced proliferation (4AS cells) and to cooperate with an anti-p55 chain mAb (33B3.1) for inhibiting IL-2 binding and proliferation.

Previous studies have indicated that high-affinity interleukin 2 receptors (IL-2R) are comprised of at least two distinct noncovalently **associated** subunits of Mr 55,000 (p55) and Mr 75,000 (p75).

These results indicate that the level of p75 is integral in determining the level of sympathetic NGF and that NGF **competes** with NT3 by increasing the expression of p75 and decreasing the expression of trkC.

In addition, our findings reveal several distinctive features of p75 mRNA and trkA mRNA expression in sympathetic neurons compared with sensory neurons and provide a plausible explanation for previously observed differences in the **effects** of a p75 null mutation on the response of sensory and sympathetic neurons during embryonic and postnatal development.

Furthermore, although no endogenous IL-2 production was detected, p75 was readily cross-**linked** to p55 for EL4J-3.4, a p55 transfectant of EL4 that bears high affinity IL-2R.

Mutation of Asp20 in human interleukin-2 (IL-2) to Lys is known to result in an IL-2 molecule with unchanged **binding** to the p55 subunit of the IL-2 receptor, but with greatly decreased affinity for the p75 subunit (Collins, L., Tsien, W.-H., Seals, C. et al. Proc. Natl. Acad. Sci USA 1988. 85: 7709).

Soluble tumor necrosis factor (TNF) receptors p55 and p75 and interleukin-10 **downregulate** TNF-alpha activity during the lung response to silica particles in NMRI mice.

We tested the hypothesis that p75 is involved in this sympathetic sprouting by comparing sprouting following sciatic nerve **cut** in wild-type (CD1) and p75 knockout mice.

Antibody-mediated blockade of CD120a (p55) completely **inhibited** NO2- expression in response to TNFalpha, whereas blockade of CD120b (p75) reduced NO2-accumulation by approximately 50%.

TNFR-1 (p55) and Fas share a death domain which is critical for apoptosis signaling whereas TNFR-p55 and TNFR-2 (p75) can **activate** NF-kappaB leading to anti-apoptotic proteins expression such

as A1.

Specific antibody-mediated aggregation of CD120a (p55) **induced** NO2- accumulation in culture supernatants and iNOS mRNA expression in macrophage lysates, whereas cross-linking of CD120b (p75) had a minimal effect.

In the ob/ob mice, the absence of p55 caused a significant improvement in insulin sensitivity. p75 deficiency alone did not affect insulin sensitivity but might potentiate the **effects** of p55 deficiency in animals lacking both TNFRs.

Specific ligation of CD120a (p55) with either (i) human TNFalpha or (ii) by incubation with mouse TNFalpha following pretreatment of macrophages with **blocking** concentrations of anti-CD120b (p75) antibody resulted in a similar reduction in NO2- production in response to TNFalpha.

We thus studied the effect of reduced glutathione (GSH) and N-acetyl-cysteine (NAC) on IL-12 p75 production by human THP-1 cell **stimulated** with IFN-gamma and Staphylococcus aureus Cowan strain I (SAC), using ELISAs specific for IL-12 p75 or the p40 subunit.

Animal experiments comparing the tetravalent and bivalent p55 fusions and the **effects** of the CH1 domain did not show significant differences in their ability to protect mice from endotoxin-induced lethality, although the p55 fusion proteins appeared to be more protective than the p75 fusion proteins.

The similarity of the relationship between this intramembrane p75 and/or Ly6C and the cytoplasmic Fgr to the relationships previously reported between T cell antigen receptor **complex** including CD4 and CD8 coreceptors, and Lck or Fyn in T cells and between surface IgM and Lyn or Blk in B cells suggested that the Fgr and p75 or Ly6C are indeed associated each other and responsible for recognition of extracellular substances (either cellular or non-cellular) and for signal transduction.

While alpha p55 injected i.c.v. **induced** a marked elevation in CS and IL-6, alpha p75 induced CS (although less than alpha p55) but no IL-6. rmTNF, which binds both receptors, was more potent in inducing IL-6 and CS than injection of rhTNF, which in mice binds only p55.

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TrkA and mitogen-**activated** protein kinase phosphorylation are **enhanced** in sympathetic neurons lacking functional p75 neurotrophin receptor expression.

Overexpression of Rab3B mutants **inhibited** the cell-surface **transport** of LDLR, but not p75NTR and Claudin-1.

These data indicate an initiating role of ceramide generated by neutral sphingomyelinase in the diverse neuronal responses **induced** by **binding** of neurotrophins to p75.

The role of the p75 nerve growth factor receptor in the retrograde **transport** of neurotrophins in the adult CNS was investigated by comparing the **transport** of 125I-labeled neurotrophins by normal and p75 nerve growth factor receptor-deficient cholinergic septohippocampal neurons.

Human TNFalpha **binds** to and **activates** the murine p55 receptor, but not the p75 receptor.

Tumor necrosis factor (TNF) **promotes** multiple aspects of allograft rejection via **binding** to type 1 (p55) and type 2 (p75) receptors.

The only molecular mechanism proposed thus far to explain this effect

is the process of "ligand passing," whereby TNF is concentrated at cell surfaces by **binding** to p75 and then following dissociation from this receptor class **binds** with high efficiency to p55.

Receptor binding studies suggested that neutralization resulted from cA2 **blocking** of TNF **binding** to both p55 and p75 TNF receptors on the cells.

Studies on the formation of high-affinity IL-2 **binding** sites of an IL-2 receptor p55 + p75 heterodimeric **complex**: functional importance of a determinant on the p55 subunit defined by a monoclonal antibody AHT-107.

Moreover, the effect of cAMP on IL-2 **binding** to p75 subunits is post-transcriptional, because the steady state levels of p75 mRNA expression are not altered within a time interval that **produced** nearly a 50% reduction in p75 binding.

The aim of this work was to study the relative role of the two TNF receptors (p55 and p75) in the central actions of TNF, studying the elevation of serum corticosterone (CS) and IL-6 levels after injection of recombinant murine (rm)TNF (intracerebroventricularly (i.c.v.)) in normal or p55-deficient (p55 -/-) mice. rmTNF **induced** high serum IL-6 levels and doubled serum CS in normal mice, whereas no elevation of serum IL-6 or CS was **induced** in p55 -/- mice.

Inhibition could be mediated by either the **p75NTR** or TrkA receptor.

Primary olfactory axons form ectopic glomeruli in mice lacking **p75NTR**.

Apoptosis induced by **p75NTR** overexpression requires Jun kinase-dependent phosphorylation of Bad.

At birth, and at 6 weeks of age, afferent fibers are intensely immunoreactive for both **p75NTR** and TrkC.

High-dose NGF may induce cytoplasmic relocation of the receptor TrkA and axonal growth arrest independently of **p75NTR**.

After a perinatal switch, however, Merkel cells in whiskers of newborn mice are immunoreactive for **p75NTR**, TrkC and NT-3.

The aim of this study was to determine whether neural precursors in vivo show cell cycle phase-dependent changes in expression of **p75NTR** and Ret.

However, no promotion of neuronal commitment by BDNF was observed in the neural precursor cells from mice carrying a mutation in the **p75NTR** gene.

These observations suggest that neurotrophins regulate filopodial dynamics by depressing the activation of RhoA that occurs through **p75NTR** signaling.

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We have studied disease progression of hSOD1 (G93A) mice in the absence of the **p75NTR** receptor and we monitored histological changes in the ventral spinal cord.

The common neurotrophin receptor (**p75NGFR**) can signal in vitro through activation of the c-Jun N-terminal kinase (JNK) pathway and nuclear translocation of NFKappaB.

When the same series of tumor cells were injected into the flanks of SCID mice, the growth of prostate tumors was suppressed in proportion to increased **p75NTR** expression.

Overexpression of this fragment in heterologous cells results in

activation of Jun kinase and induces Pro-caspase-3 cleavage, indicating that it activates **p75NTR** signaling cascades.

We examined the hypothesis that hyperglycemia-induced changes in Cav-1 expression and **p75NTR** signaling may contribute to altered neurotrophism in DPN by modulating SC responses to neuregulins.

Cellular colocalization also revealed **p75NTR** immunoreactivity on neighboring blood vessels and cells in the injured nerve, but not on activated GFAP+ astrocytes or alphaMbeta2+ microglia and macrophages.

On the other hand, digoxigenylated 192IgG was found to be an excellent immunocytochemical marker for **p75NTR** as shown by double labelling including highly sensitive mouse antibodies directed against ChAT.

These data further reveal that an absence of **p75NTR** function in trigeminal sensory neurons does not diminish their capacity for NGF-dependent plasticity, namely trkA mRNA expression and collateral growth of central afferent axons.

Explants cultured with glial-derived neurotrophic factor (GDNF) exhibited a striking increase in the amount of **p75NTR**- and PGP 9.5-positive tissue outside the lobes, whereas GDNF-impregnated beads attracted neuronal precursors and influenced the direction of neurite extension.

In this study, we show that overexpression of **p75NTR** in primary cortical neurons, in pheochromocytoma cell line (PC12) cells, and in glioma cells results in activation of Jun kinase (JNK), accumulation of cytochrome c within the cytosol, and activation of caspases 9, 6, and 3.

Stimulated **p75NTR** shedding is abrogated in M2 mutant Chinese hamster ovary cells that lack functional tumor necrosis factor-alpha converting enzyme (TACE, also referred to as ADAM17) and in cells isolated from adam17-/- mice, but not in cells from adam9/12/15-/- or adam10-/- mice.

We report here that the spatial and temporal expression of **p75NTR** is included in Necdin expression domain.

Experiments with p75NTR-null mutant mice showed that immediate Rho activation after SCI is **p75NTR** dependent.

The p75 receptor for TNF and intercellular adhesion molecule 1 have a negligible role in this toxic shock model.

The promoter region of the murine p75 TNF receptor (TNF-R) was isolated from a mouse genomic DNA cosmid library.

BDNF is present in the pineal gland during target innervation, and incoming sympathetic axons are **p75NTR** positive.

In cultured neonatal sympathetic neurons, p53 protein levels are elevated in response to both NGF withdrawal and **p75NTR** activation.

We show that **p75NTR** is expressed at highest levels in the region of the cerebellum where foliation is altered in BDNF and NT3 mutants.

Absence of **p75NTR** causes increased basal forebrain cholinergic neuron size, choline acetyltransferase activity, and target innervation.

Nerve growth factor blocks the glucose-induced down-regulation of caveolin-1 expression in Schwann cells via p75 neurotrophin receptor signaling.

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Preliminary results suggest that upregulation of the soluble p75 TNF receptor may be one mechanism by which TNF-alpha bioactivity reduction occurs.

Reductions in p75NTR expression and subsequent caspase-3 activation in spinal cords were consistent with increased survival in antisense PNA-treated mice.

Neurotrophins (NTs) bind to two different classes of cell surface receptors, Trk receptor tyrosine kinases and p75NTR, both of which are expressed by neuroblastoma cells.

Here, we investigated whether and when the cholinergic neurons of the neostriatum, which express TrkA and p75NGFR during early postnatal times, undergo p75NGFR-mediated death.

Although neither TrkA nor p75NTR was detectable in either HCC or normal hepatic cells, TrkA was shown in the walls of tumor-associated arteries that contain abundant nerve fibers.

Post-ganglionic sympathetic neurons from postnatal day 1 p75NTR exon III null mutant (p75(-/-)) and 129/SvJ mice were cultured in the presence of 50 ng/mL NGF and analysed by Western blotting.

When 70W cells were exposed to antisense oligonucleotides directed against p75NTR mRNA, there was a reduction in NGF and NT-3 binding, and the neurotrophins failed to enhance Matrigel invasion.

To investigate this further, we examined the consequences of peripheral immune stimulation without specific autoantigen in wild-type or transgenic (termed GF-IL12) mice with astrocyte production of the bioactive IL-12 p75 heterodimer.

We measured APP products and mRNAs for NGF and its low-affinity receptor p75 in 10-month-old Tg2576 whole brain after dietary propentofylline (PPF) or acetyl-L-carnitine (ALCAR) for 4 weeks to induce NGF- or p75-expression, respectively.

Enhanced tyrosyl phosphorylation of p75 is also seen when cells overexpressing c-src are treated with platelet-derived growth factor (PDGF), but significantly less phosphorylation is observed with insulin and fibroblast growth factor (FGF).

In order to gain insight into specific roles for TrkC NC2 receptors during CNS neurogenesis, we compared its distribution with that of its catalytic counterparts and the p75NTR receptor in in vivo and in vitro model systems of early and late neuronal differentiation.

Using antisera that recognize undifferentiated neural-crest-derived cells (p75NTR) and differentiated neurons (PGP9.5), we examined the colonisation of the murine large intestine by neural-crest-derived cells and the development of the myenteric and submucosal plexuses.

We have used immunofluorescence techniques with a panel of antibodies against known neurotrophin receptors (trk A, trk B, trk C, p75NTR) to map the locations of these receptors in the developing neuromuscular system of mice from our neurotrophin-3 (NT-3) knockout colony.

Comparisons of calcitonin gene-related peptide immunoreactivity in the dorsal horn revealed that the area occupied by DRG central processes was not significantly different between p75NTR hypomorphic mice and wild-type siblings, or between NGF transgenic mice with either hypomorphic or normal expression of p75NTR.

In these mice, cells expressing cholinergic neuron markers, such as choline acetyltransferase, vesicular acetylcholine transporter and p75

low-affinity **NGF receptor**, were markedly reduced in the basal forebrain, whereas other cholinergic neurons including brain stem and spinal motor neurons expressed the markers.

Studies from this laboratory have shown that the interstitial population of mesenchymal cells in fetal and newborn mouse testis express the p75 neurotrophin receptor (**p75NTR**, formerly known as the low-affinity nerve growth factor receptor); part of the cell population progressively congregates around testis cords, later to be replaced by contractile peritubular myoid cells, which express smooth muscle cell markers.

In both animal models absence of **p75NTR** led to a twofold, early increase in the number of CD3+.

To a lesser extent, p75 decreases Abeta peptides, possibly via peptidases since sAPPalpha level is not changed.

No significant changes in NgR mRNA levels were observed in jimpy, where the increase in p75 level can be correlated with the cell death of oligodendrocytes.

Analysis of a neural crest marker, p75, in rae28-deficient mice revealed that the neural crest cells begin to ectopically express Hoxb3 after leaving the hindbrain.

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Mice with a targeted deletion of the low-affinity neurotrophin receptor p75 (p75-/-) exhibit a 50% loss of large- and small-diameter sensory neurons in the dorsal root ganglion.

Low-affinity nerve growth factor receptor (p75NGFR)- and choline acetyltransferase (ChAT)-immunoreactive axons in the cerebral cortex and hippocampus of adult macaque monkeys and humans.

In contrast, exacerbated pulmonary inflammation and dramatically increased endotoxin induced serum TNF levels in mice lacking p75 suggest a dominant role for p75 in suppressing TNF-mediated inflammatory responses.

The induction of **p75NTR** expression in mature degenerating spinal motor neurons of humans and transgenic mice with amyotrophic lateral sclerosis (ALS) suggests a role of **p75NTR** in the progression of motor neuron disease (MND).

During cyclophosphamide-induced follicle dystrophy and alopecia, massive keratinocyte apoptosis occurred in the entire proximal hair bulb, except in the dermal papilla, despite a strong up-regulation of Bax and **p75NTR** immunoreactivity.

Here, we demonstrate that mice exposed to CSH from P3 to P33 followed by normoxia from P33 to P75 continue to exhibit a locomotor hyperactivity that resembles behavioral changes observed in some human children with very low birth weights.

Next, we examined the role of the p75 neurotrophin receptor (**p75NTR**) in Rho signaling.

Mutants in the BDNF receptor gene trkB and antibodies to its second receptor **p75NTR** have been used to determine the receptors and cells involved in this response.

The chemical properties of p75 and its expression by the cell types so far examined indicate that p75 is a possible candidate for the guinea-pig homologue of the murine Lyt-1 antigen.

Moreover, neuroprotection by NGF against glutamate toxicity was abolished in **p75NTR**-/- neurons, and the expression of bcl-2 and bcl-xl was markedly reduced as compared to wildtype cells.

The immunoreactivities of NPY, tyrosine hydroxylase, and **p75** low affinity **NGF receptor** in nerve terminals within the mesenteric artery were also reduced, whereas that of the sensory neuron neuropeptide, calcitonin gene related peptide was less affected.

Indeed, expression of CRB3 or of a chimera containing the extracellular domain of the neurotrophin receptor **p75NTR** and the transmembrane and cytoplasmic domains of CRB3 led to a slower development of functional tight junctions in Madin-Darby canine kidney cells.

The segregation of polymorphic alleles at and around loci for **p75NGFR**, TRKA, TRKB, BDNF, and familial dysautonomia (another hereditary sensory neuropathy having features in common with HSN II) virtually excluded these genes as the cause of HSN II in this family.

Nerve growth factor (NGF), neurotrophin-3, neurotrophin-4, and brain-derived neurotrophin exert their survival effect by binding to two transmembrane receptor types: trk receptors, which exhibit binding specificity, and the **p75NTR** receptor, which binds all neurotrophins.

In studies aimed at identifying and characterizing pp60c-src substrates that participate in the enhanced mitogenic response to epidermal growth factor (EGF) observed in murine C3H10T1/2 fibroblasts overexpressing c-src, we have identified a 75-kDa protein (**p75**) whose properties are consistent with those expected of such a substrate.

p75 neurotrophin receptor mediates neurotrophin activation of NF-kappa B and induction of iNOS expression in P19 neurons.

Conversely, mouse astrocytes do not express IL-12 p35 mRNA and do not secrete IL-12 **p75** under any condition tested.

These neurons express the 75-kDa low-affinity neurotrophin receptor (**p75NTR**) and choline acetyltransferase (ChAT), both proteins are specifically expressed by neonatal and embryonic motor neurons in vivo.

In this study, the authors used mice that overexpressed NGF (NGF-OE) or NT3 (NT3-OE) in skin and mice that lacked **p75** (**p75**(-/-)) to understand the dynamics of sympathetic neuron response to each neurotrophin and to address the role of **p75**.

NT-3/TrkC and NGF/TrkA signaling stimulate HF development, while NT-3, NT-4 and BDNF inhibit the growth (anagen) of mature HF by the induction of apoptosis-driven HF regression (catagen). **p75NTR** stimulation inhibits HF development and stimulates catagen.

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The purpose of the present study is to examine the effect of MITF on **p75** gene transcription.

Staining of the dorsal horn of the spinal cord for CGRP and IB4 was also normal in **p75**-/- animals.

Here we show that the neurotrophin receptor **p75** (p75(NTR)) is the signal transducing element for MAG.

In addition, high-fat diet-fed **p75**(-)/- mice had the lowest body weights and leptin levels, and improved insulin sensitivity.

The lesioned striatum in control-grafted animals displayed numerous **p75** neurotrophin-ir (**p75NTR**) astrocytes, which enveloped host vasculature.

4. The present findings suggest that **p75** gene deficiency disrupt an allergic airway inflammation and AHR in mice by interfering type 2 helper T (Th2) cell responses.

Although **p75** is structurally a member of the Fas/TNFR1 receptor

family, caspase-8 was not required for p75-mediated death, unlike other members of this receptor family.

We show that the marked increase in p75 and trkA mRNA expression that occurs between E11 and E13 in normal embryos takes place on time and to the same extent in NGF-/- embryos.

This means that NGF-induced hyperalgesia can occur in the absence of the p75 receptor and suggests that the trkA receptor is sufficient to mediate the acute noxious action of NGF.

During hair follicle (HF) morphogenesis, p75 neurotrophin receptor (p75NTR) reportedly is the first growth factor receptor found to be expressed by those fibroblasts that later develop into the dermal papilla (DP) of the HF.

We used quantitative reverse transcription (RT)/PCR to study the regulation of p75 mRNA and trkA mRNA expression in the developing sympathetic neurons of the mouse superior cervical sympathetic ganglion (SCG) in vivo and in vitro.

Western blot analysis showed that a protein with an approximate molecular weight of 75 kDa (p75), which was distinct from Vn, existed in the nuclear fraction, and, more specifically, in the nuclear matrix fraction, of NIH3T3 cells.

In vivo, pilocarpine-induced seizures, previously shown to up-regulate p75 expression and increase neurotrophin production, caused activation of caspase-6 and -3 and cleavage of poly(ADP-ribose) polymerase in p75-expressing hippocampal neurons.

To examine the mechanisms that underlie the neurotrophin-induced, apoptosis-driven hair follicle involution (catagen), the expression and function of p75 neurotrophin receptor (p75NTR), which is implicated in apoptosis control, were studied during spontaneous catagen development in murine skin.

NGF has the potential to stimulate the growth of some pancreatic cancer cell lines, and this effect is mediated by the phosphorylation of tyrosine kinase receptor A and mitogen-activated protein kinase activation; it is dependent on the expression levels of tyrosine kinase receptor A and p75 receptors.

Macrophages expressed NGF and the NGF receptors TrkA and p75.

cAMP regulation of IL-2 receptor expression. Selective modulation of the p75 subunit.

Both p75 and p140 molecules are known to be involved in the formation of NGF receptors.

The p75 protein, termed ZAN75, exhibited DNA-binding activity in a zinc-dependent manner.

The cells of the intercalated ducts showed p75 IR (sublingual) and TrkA IR (parotid gland).

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Cells in lymphoid aggregates expressed both TNF-R, but with a predominant expression of p75 receptor.

Monoclonal antibody defining a molecule possibly identical to the p75 subunit of interleukin 2 receptor.

Under conditions of low p75 expression, Lys-20 IL-2 could act as an antagonist of wild-type IL-2 action.

Using RT-PCR, we observed increased expression (2.4-fold) of TNF receptor 2 (p75) in the hypothalamus of obese mice.

Etanercept is a fusion protein, composed of the Fc portion of IgG1 and the extracellular domain of the TNF receptor (p75).

Monoclonal antibodies specific for murine p55 and p75 tumor necrosis factor receptors: identification of a novel in vivo role for p75.

Finally, ovariectomy caused bone loss in wt mice and in mice lacking p75 TNF receptor but failed to do so in mice lacking the p55 TNF receptor.

Finally, secretion of the IL-12 p75 heterodimer was detectable by ELISA from astrocytes treated with LPS plus IFN-gamma, but not with LPS alone.

Neurotrophin receptor-interacting MAGE (NRAGE) is the most recently identified p75 neurotrophin receptor (p75(NTR)) intracellular binding protein.

By contrast, in double knockout mice lacking both p55 and p75 receptors, the entry of (125)I-TNFalpha into brain and spinal cord was completely abolished.

Cytotoxicity in L929 murine fibrosarcoma cells after triggering of transfected human p75 tumour necrosis factor (TNF) receptor is mediated by endogenous murine TNF.

The neurotrophin receptor p75NTR is the coreceptor for Nogo receptor, mediating growth cone collapse in vitro by MAG, myelin oligodendrocyte glycoprotein (Omgp), and Nogo.

Furthermore, we have shown that the insolubilised synthetic peptide corresponding P-ITIM bound Shc, Lyn and the p75 and p 10 unidentified tyrosine phosphorylated proteins.

Furthermore, p75NTR/NADE-induced cell death was dependent on NGF but not BDNF, NT-3, or NT-4/5, and the recruitment of NADE to p75NTR (intracellular domain) was dose-dependent.

In p75(-/-) mice, no activated caspase-3 was detected, and there was a marked reduction in the number of dying neurons after pilocarpine treatment compared with wild type mice.

Transcytosis of 125I-TNF-alpha across a monolayer of the cerebral endothelial cells that compose the blood-brain barrier was significantly reduced in the absence of functional p55 and p75 receptors.

PURPOSE: To investigate the distribution of p75 and p55 tumor necrosis factor receptor (TNFR) mRNA in normal mouse eyes and in mouse eyes acutely infected with McKrae strain herpes simplex virus (HSV).

The effect of TNF alpha is mediated by two membrane receptors carried on the surface of target cells (TNF-RI p55 and TNF-RII p75) which are released into the biological fluids (synovial fluid and plasma).

Furthermore, given the species-specific nature of the mouse p75 TNF receptor, it is assumed that the pathology induced by human TNF in these transgenic mice is associated exclusively with p55 TNF receptor signaling.

To better understand the role of the p75 receptor in the events following nerve injury, we have compared apoptosis in injured sciatic nerves of adult mice lacking functional p75 receptors and Balb-C (wild-type) mice.

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Both a nontumorigenic clone, B2BE2, and a tumorigenic clone, B2BE6,

expressed comparable amounts of gp185erbB-2, which became phosphorylated on tyrosine in response to treatment with the c-erbB-2 ligands gp30 and p75.

Expression of the neurotrophin receptor p75 receptor coincides with the expression of activating transcription factor 3, a member of the activating transcription factor/cyclic AMP family of stress transcription factors.

Aside from well-described dopamine and serotonin receptor blockade effects, clozapine may also be neuroprotective through its modulation of the p75 neurotrophin receptor (p75(NTR)) and superoxide dismutase 1 (SOD1) expression.

In dissociated cultures of sympathetic neuroblasts, retinoic acid inhibited the developmental increase in trkA mRNA expression and the developmental decrease in trkC mRNA expression that normally occurs in these cells but did not affect p75 mRNA expression.

The 75-kDa protein was purified and analyzed by matrix-assisted laser desorption ionization time-of-flight mass spectrometry followed by postsource-decay profiling. p75 is a novel type I transmembrane protein of the Ig superfamily which is most similar to FPRP.

Verifying that TNF is essential to development of particle osteolysis, mice failing to express both the p55 and p75 TNF receptors are protected from the profound bone resorption attending polymemthyl-methacrylate particle implantation on calvariae of wild-type animals.

Nerve growth factor receptor p75 (NGFR) gene was investigated as a potential candidate gene in Meckel syndrome (MKS) because of its important role in embryonic development, chromosomal localization adjacent to the MKS locus and Meckel syndrome-resembling findings in knock-out mice phenotype.

Neurotrophin binding to the p75 receptor modulates Rho activity and axonal outgrowth.

Differentiating enteric neurons showed high Ret, low p75, and undetectable Sox10 immunostaining.

Necdin-related MAGE proteins differentially interact with the E2F1 transcription factor and the p75 neurotrophin receptor.

We tested this hypothesis by instilling E. coli into the lungs of wild-type (WT) mice and gene-targeted mice that lack both p55 and p75 receptors for TNF-alpha.

METHODS: We performed a contact hypersensitivity (CHS) assay on gene-targeted mutant mice (TNFR1R2-/-) lacking genes for both receptors (p55 and p75) for TNF-alpha.

In contrast, mice with targeted deletion of the p55 or p75 TNF receptor, or of interleukin-18, displayed normal or higher pain sensitivity compared to their respective controls.

We conclude that the neural crest cell population that arises from the vagal level of the neural axis and that populates the stomach, midgut, and hindgut expresses Phox2b, Ret, and p75.

In accordance with previous data, we also find neurotrophins in the targets of sensory neurons (skin) and motoneurons (muscle) and the neurotrophin receptors p75, trkA, and trkB in sensory and sympathetic ganglia.

The location and sequence of appearance of enteric neuron precursors deduced from the explants grown under the kidney capsule or in organ culture was very similar to that seen with the Phox2b, Ret, and p75 antisera.

Among many MAGE proteins, magphinins are closely related to NRAGE, which mediates p75 neurotrophin receptor-dependent apoptosis, and necdin, which is a strong suppressor of cell proliferation in post-mitotic neurons.

To elucidate the role that specific proinflammatory cytokines play in the induction of this process we examined the development of EAE in mice with targeted disruptions of the TNF p55 or p75 or the IL-1 p80 receptors.

All three types of mice (p55 deficient, p75 deficient, and normal) showed comparable rises in the levels of two acute-phase proteins (serum amyloid P and C3) at 24, 48, and 72 h after the experimental infections, and all of the mice showed comparable influxes of neutrophils to the site of infection.

TNF-alpha signaling through the p55 receptor (but not the p75 receptor) is crucial in resisting S. pneumoniae infections, because intraperitoneal injection of 100 CFU/mouse killed p55-deficient mice by day 2 of infection, whereas 1,000,000 CFU/mouse was needed to kill half of the control mice. p55-deficient mice do not show evidence of a deficient acute-phase response.

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The p75 receptor transduces the signal from myelin-associated glycoprotein to Rho.

Mice deficient in tumor necrosis factor receptors p55 and p75, interleukin-4, or inducible nitric oxide synthase are susceptible to endotoxin-induced uveitis.

We have extended these studies to investigate the induction of p75 tumour necrosis factor receptor (TNF-R) shedding, another anti-inflammatory property of IL-10.

In the thymus the p75 receptor was confined to medullary lymphoblasts and dendritic cells, which co-stain with the Tac protein of the interleukin-2 (IL-2) receptor.

These results suggest that the hypothalamic TNF receptor 2 (p75) might play a role in obesity by modulating the actions of TNF-alpha in conditions of leptin resistance.

Moreover, mice lacking p55 receptors exhibited increased degeneration of CA3 hippocampal neurons after administration of the excitotoxin kainic acid compared with wild-type mice and mice lacking p75 receptors.

These results are consistent with a mechanism by which IL-4 can prime T cells and certain thymocytes for responsiveness to IL-2 by increasing IL-2R p75 chain gene expression, independent of general T cell activation.

Here we examined their roles in regulating the cell-surface transport of apical p75 neurotrophin receptor (p75NTR), basolateral low-density lipoprotein receptor (LDLR), and tight junctional Claudin-1 using transport assay in non-polarized fibroblasts.

The enhancement of chemotactic response and heparanase production was detected at NGF concentrations sufficient to fully saturate both low- and high-affinity NGF receptors (NGFR), the neurotrophin receptor (p75) and the trkA gene product, respectively.

Pretreatment with 250 micrograms of the p75 construct delayed but did not avert death in this model, reducing peak bioactive TNF-alpha levels after infection from 76.4 ng ml-1 in control mice to 4.7 ng ml-1 in the treated group ($p < 0.05$, two-sample t test).

Contact with the tumor cells stimulated NK cells to proliferate, secrete IFN-gamma, TNF-alpha, and soluble IL-2R, up-regulate cell surface expression of IL2R p55 and p75 as well as CD16 Ag, and mediate higher levels of antitumor activity in 51Cr-release assays.

The domain structure of DAMAGE is similar to that of NRAGE, a MAGE protein that mediates p75 neurotrophin receptor signaling and neuronal apoptosis (Salehi, A. H., Roux, P. P., Kubu, C. J., Zeindler, C., Bhakar, A., Tannis, L. L., Verdi, J. M., and Barker, P. A. (2000) Neuron 27, 279-288).

The p75 low-affinity neurotrophin receptor (p75(LNTR)) appears to have various functions that include enhancing nerve growth factor (NGF)-mediated survival by increasing TrkA (high-affinity NGF receptor) efficiency, and mediating apoptosis by acting as a ligand-regulated pro-apoptotic receptor.

In addition, NGF induced autophosphorylation of TrkA and could substitute for granulocyte-monocyte colony-stimulating factor to trigger the proliferation of the TF1 cell line, with a half-maximal signal observed at 50 pmol/L, indicating that p75 is not required for DNA synthesis in this cell line.

The major products of translation of full-size 35S polyadenylylated virion RNA were gag-related polyproteins of 75,000, 105,000, and 180,000 daltons (P75, P105, and P180, respectively).

Overexpression of p75 translocated necdin and MAGE-G1 in the proximity of the plasma membrane and reduced their association with E2F1 to facilitate E2F1-induced death of neuroblastoma cells.

Transfected NIH 3T3 cells express two 3611-MSV-specific polyproteins (P75 and P90), both of which contain NH2-terminal gag gene-encoded components linked to the acquired sequence (v-raf) translational product.

However, it should be kept in mind that cytokines were also argued to provide beneficial effects in brain injury as inferred from studies with TNF-receptor knock-out mice (p55 and p75 knock-out), which display increased sensitivity to brain ischemia, and the capacity of IL-1 to elicit the state of ischemic tolerance upon repeated administration.

In contrast, p75(-/-) knockout mice exhibited exacerbated EAE, enhanced Th1 cytokine production, and enhanced CD4(+) and F4/80 (+) CNS infiltration.

Expression of p75, TrkA, TrkB and TrkC was examined in mouse retinas by means immunohistochemistry in the postnatal development of normal and rd/rd mice (C57BL/6J).

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IL-2 receptor expression in autoimmune MRL-lpr/lpr mice. The expanded L3T4-, Lyt-2- population does not express p75 and cannot generate functional high-affinity IL-2 receptors.

Here we show by microsequencing that the peptides derived from the purified p75 and p85 subunits of NHP1 from HeLa cells have between 64 and 100% identity with the human Ku autoantigen.

This study was undertaken to analyze the occurrence of low- (p75) and high-affinity (TrkA, TrkB and TrkC) neurotrophin receptor proteins in human and mouse salivary glands using immunohistochemistry.

Tumour necrosis factor (TNF), jointly referring to TNF alpha and TNF beta, is a central mediator of immune and inflammatory responses; its activities are mediated by two distinct receptors, TNFR1 (p55) and TNFR2 (p75) (reviewed in refs 1-3).

Furthermore, we correlated MMP-13/TIMP-1 RNA abundance with activation of the transcription factors AP-1 and NF-kappaB in the lungs of C57BL/6 mice, and of mice deficient in one of the two types of TNFR (p55(-/-) or p75(-/-)), exposed to silica (0.2 g/kg) or saline by intratracheal instillation.

Recently, it was reported that the IL-2R (whose p75 beta-subunit shares sequence homology with a known murine IL-3R subunit and a common beta-subunit of the human IL-3R and granulocyte-macrophage colony-stimulating factor [GM-CSF] receptors) can physically associate with and regulate the activity of the SRC-family PTK, p56-LCK.

LPS induces secretion of IL-12 p40, but not of IL-12 p75, as detected by specific ELISA.

Of these, only p75 and a trace of p85 were detected, by immunoblotting, in extracts derived from ML-1 cell nuclei.

Silica upregulated expression of the p75 receptor, but not the p55 receptor, in the C57BL/6, BALB/c, and 129/J mice.

The p75 neurotrophin receptor serves as a receptor for all known neurotrophins, including NGF, BDNF, NT-3, and NT-4/5.

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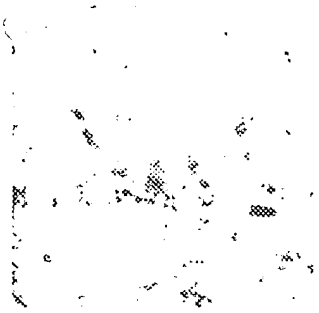

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A role for p75 neurotrophin receptor in the control of apoptosis-driven hair follicle regression.

To examine the mechanisms that underlie the neurotrophin-induced, apoptosis-driven hair follicle involution (catagen), the expression and function of p75 neurotrophin receptor (p75NTR), which is implicated in apoptosis control, were studied during spontaneous catagen development in murine skin. By RT-PCR, high steady-state p75NTR mRNA skin levels were found during the anagen-catagen transition of the hair follicle. By immunohistochemistry, p75NTR alone was strongly expressed in TUNEL+/Bcl2- keratinocytes of the regressing outer root sheath, but both p75NTR and TrkB and/or TrkC were expressed by the nonregressing TUNEL-/Bcl2+ secondary hair germ keratinocytes. To determine whether p75NTR is functionally involved in catagen control, spontaneous catagen development was compared in vivo between p75NTR knockout (-/-) and wild-type mice. There was significant catagen retardation in p75NTR knockout mice as compared to wild-type controls ($P<0.05$). Instead, transgenic mice-overexpressing NGF (promoter: K14) showed substantial acceleration of catagen ($P<0.001$). Although NGF, brain-derived neurotrophic factor (BDNF), and neurotrophin 3 (NT-3) accelerated catagen in the organ-cultured skin of C57BL/6 mice, these neurotrophins failed to promote catagen development in the organ-cultured p75NTR null skin. These findings suggest that p75NTR signaling is involved in the control of kerotinocyte apoptosis during catagen and that pharmacological manipulation of p75NTR signaling may prove useful for the treatment of hair disorders that display premature entry into catagen.

FASEB JOURNAL (2000-10-01)

PMID: 11023977